

**In the Claims:**

Please add new claim 16 as follows.

- A1 16. (new) The pharmaceutical composition of claim 15, wherein said endorepellin protein is between 210 amino acids and 705 amino acids in size.

**In the Description of the Drawings:**

Please substitute the five paragraphs of the Description of the Drawings starting on page 3, line 16 "Figure 1. Perlecan . . ." and ending on page 5, line 28 ". . . represent the mean +/- SE (n=4)." with the following substitute paragraphs.

A2 **Figure 1.** Perlecan domain V (endorepellin) binds to the anti-angiogenic factor endostatin. Figure 1a, Agarose gel showing the 1.7 kb cDNA strongly interacting with endorepellin, obtained from the BglII digestion of clone A3. Complete sequence of A3 clone revealed the C terminus of type XVIII collagen. Figure 1b, Schematic representation of the human  $\alpha$  chain of type XVIII collagen. The triple-helical and non-triple helical domains are indicated by rods and blue boxes, respectively. The C-terminal endostatin fragment is highlighted in orange. The beginning of the clone A3 sequence is shown (NCBI accession # AF018082). Figure 1c, Growth and  $\beta$ -galactosidase activity triggered by the interaction of endorepellin with collagen type XVIII fragment compared to the positive (p53 and T-antigen) and negative control (lamin and T-antigen). Figure 1d, Co-immunoprecipitation of collagen XVIII (clone A3) and endorepellin following *in vitro* transcription/translation using [ $^{35}$ S]methionine as the labeled precursor. Endorepellin (lane 1) and collagen XVIII (lane 2) are mixed in equimolar amounts and co-immunoprecipitated with either anti-hemagglutinin ( $\alpha$ -HA) (lane 3) or no antibody. Figure 1e, Co-immunoprecipitation of endostatin with endorepellin. Domain III (lane 1), endorepellin (lane 2) and endostatin (lane 3) were generated by *in vitro* transcription/translation using [ $^{35}$ S]methionine as the labeled precursor. Endostatin was mixed with either domain III (lane 4) or endorepellin (lane 5) and immunoprecipitated with anti-hemagglutinin ( $\alpha$ -HA) antibody. Figure 1f, Schematic representation of domain V and various deletion mutants. Orange ovals indicate laminin-type G modules (LG), whereas blue rectangles indicate EGF-like (EG) modules. The

growth is indicated by semi-quantitative assessment with maximal growth at +++. The numbers within parentheses designate the amino acid position based on the mature protein core. Figure 1g, Representative  $\alpha$  and  $\beta$ -galactosidase assays of various deletion mutants, as indicated; pGB53/pGADT was the positive control.

**Figure 2.** Endorepellin is a powerful anti-angiogenic factor. Figure 2a, Purification of endorepellin from media conditioned by 293-EBNA cells expressing the 81 kDa endorepellin tagged with His6. Coumassie-stained SDS-PAGE (left) and Western immunoblotting with anti-His6 antibody (right) of negative control media (lanes 1 and 4), flow through (lanes 2 and 5), and 250 mM imidazole eluate (lanes 3 and 6). Figure 2b and Figure 2c, HUVEC migration assays through fibrillar collagen using 10 ng/ml VEGF as a chemotactic inducer and preincubation the HUVECs for 30 min with various concentrations of endostatin (ES) and endorepellin (ER). Serum free medium (SFM). Figure 2d, CAM assays three days after the application of sponges containing VEGF (1 ng), VEGF (1 ng)+ endorepellin (400 ng), or buffer alone. Scale bar, 1 mm.

**Figure 3.** Endorepellin, but not endostatin, blocks endothelial tube formation induced by fibrillar collagen. Figure 3a, Figure 3b, Figure 3c, and Figure 3d, Gallery of light micrographs capturing the time course production of HUVEC tube-like formation in fibrillar collagen containing either buffer (Control), endorepellin, endostatin, or both at the designated concentrations. In this assay,  $4 \times 10^5$  cells are incubated for 24 hr and pictures are taken at various intervals as indicated in the top margins. Scale bar, 250  $\mu$ m.

**Figure 4.** Biological consequences of endostatin/endorepellin interaction. Figure 4a and Figure 4b, HUVEC migration assays through fibrillar collagen using 10 ng/ml VEGF as a chemotactic inducer and preincubation the HUVECs for 30 min with various concentrations of endostatin (ES), endorepellin (ER), or various combinations as indicated. The values are presented as the percentage of maximal stimulation induced by VEGF alone, arbitrarily set at 100%. Figure 4a is the summary of three independent experiments run in quadruplicates, mean  $\pm$ SE. The values in Figure 4b derive from an additional experiment run in quadruplicate, mean  $\pm$ SE. Serum free medium (SFM).